

REMARKS

Claims 1-9 are currently pending. As a result of the previous Restriction Requirement, Claim 10 is withdrawn from consideration as a non-elected invention. Claim 1 and the specification are amended herein, and new Claims 11-30 are added. Support for each amendment and each new claim is found in the specification as detailed herein, therefore no new matter is added to this application.

According to the Office Action of March 13, 2002, the Examiner has considered only Claims 1, 2 and 8 of the elected invention, and has not considered Claims 3-7 and 9 which constitute non-elected species, however, these claims remain pending.

Clerical Errors in Specification and Claims as Filed

The amendment to Claim 1 and the corresponding section of the specification (page 21, line 21-page 22, line 30) is as follows. First, hydrogen atoms are missing from the -ene functionalities, specifically  $-\underline{\text{CH}}=\text{CH}-\text{R}$  and  $-\text{R}-\underline{\text{CH}}=\text{CH}_2$ , in section b of the compound description (page 22, line 1) as well as Claim 1. These clerical errors are corrected by this amendment. One of ordinary skill would readily recognize this clerical error from the requirement for a hydrogen atom to satisfy the valence of each carbon to which it is bonded.

Second, possible selections for  $\text{R}_a$ , namely, where  $\text{R}_a$  is  $-\text{OC}(\text{O})\text{CH}_3$ ,  $-\text{C}(\text{O})\text{H}$ ,  $-\text{NH}_2$ ,  $-\text{NMe}_2$ , or  $-\text{NHMe}$ , which appeared in the specification, are now included in Claim 1. Support for these  $\text{R}_a$  substituents is found as follows. Support for  $\text{R}_a$  being  $-\text{OC}(\text{O})\text{CH}_3$  is found at page 20, lines 5 and Table 1. Support for  $\text{R}_a$  being  $-\text{C}(\text{O})\text{H}$  is found at page 20, lines 5 and Table 1. Support for  $\text{R}_a$  being  $-\text{NH}_2$  is found at page 20, line 6. Support for  $\text{R}_a$  being  $-\text{NMe}_2$  is

found at page 20, lines 6 and 9-10. Support for R<sub>a</sub> being -NHMe is found at page 20, lines 6 and 9-10.

Third, the missing subscript 2 is added to the nitrogen substituent Y in NY<sub>2</sub> in Claim 1 and in the corresponding section of the specification (page 22, line 17, 4<sup>th</sup> full paragraph), to indicate the amine functionality, and further clarified that Y is independently selected from the listed substituents. Again, one of ordinary skill would readily recognize this clerical error from the fact that oxygen and sulfur require a single substituent Y, specified by O-Y and S-Y, while nitrogen requires two such substituents to satisfy its valence, hence NY<sub>2</sub>. Support for this clerical correction is also found in the specification (*see, for example*: page 20, lines 6-7; Examples 13-22; Table 2, page 33).

Fourth, the deletion of the substituent >C=N-OH from the definition of Z'' in Claim 1 and in the corresponding section of the specification (page 22, line 24, 5<sup>th</sup> full paragraph) is made to remove a redundancy in Claim 1 and the specification. Thus, Z'' may be >C=N-OR<sub>5</sub> and R<sub>5</sub> may be defined, among other things, as hydrogen. Therefore, removing this redundant substituent does not change the scope of this claim, nor add new matter.

Fifth, the amendment to Claim 9 reflects the correction of a clerical error in which a carbon atom was inadvertently used in place of a nitrogen atom in the dimethylamino alkyl group. One of ordinary skill would recognize that a carbon atom cannot satisfy its valence by bonding to two methyl groups, but a nitrogen atom can. Moreover, the dimethylamino alkyl group finds support in the specification on page 22, line 17, (4<sup>th</sup> full paragraph), Claim 1, and on page 20, lines 7 and 9-10.

**Support for New Claims in Specification**

By this amendment, new Claims 11-30 are added. Support for each new claim is found in the specification as follows.

Support for new Claim 11 is found in Claims 1 and 10 as filed.

Support for new Claim 12 is found at page 20, line 5, and Table 1, page 20.

Support for new Claim 13 is found at page 20, line 5, and Table 1, page 20.

Support for new Claim 14 is found at page 20, line 5, and Table 1, page 20.

Support for new Claim 15 is found at page 20, line 6.

Support for new Claim 16 is found in Claims 1 and 10 as filed.

Support for new Claim 17 is found in Claims 1 and 10 as filed.

Support for new Claim 18 is found in Claims 1 and 10 as filed.

Support for new Claim 19 is found in Claims 1 and 10 as filed.

Support for new Claim 20 is found at page 20, lines 6 and 9-10.

Support for new Claim 21 is found in Claims 1 and 10 as filed.

Support for new Claim 22 is found in Claims 1 and 10 as filed.

Support for new Claim 23 is found in Claims 1 and 10 as filed, page 20, lines 4-12 and Table 1, in which compounds where both  $R_{h1}$  and  $R_{h2}$  are H are disclosed.

Support for new Claim 24 is found in Claims 1 and 10 as filed.

Support for new Claim 25 is found in Claims 1 and 10 as filed.

Support for new Claim 26 is found in Claims 1 and 10 as filed.

Support for new Claim 27 is found in Claims 1 and 10 as filed.

Support for new Claim 28 is found in Claims 1 and 10 as filed.

Support for new Claim 29 is found in Claims 1 and 10 as filed.

Support for new Claim 30 is found in Claims 1 and 10 as filed.

Accordingly, these amendments do not affect the scope of the claims, nor add new matter to the application.

Claim Rejections under 35 U.S.C. § 102 in View of Nambara et al.

Nambara et al. (DN 82:43650). Claims 1, 2 and 8 of the elected invention stand rejected under 35 U.S.C. § 102(b) as being anticipated by Nambara et al. (DN 82:43650; Abstract of Chem. Pharm. Bull. 1974, 22(10), 2455-7). It is the Examiner's position that Claims 1, 2 and 8 read on compounds RN 54502-29-3 and 54502-31-7 (shown on page 14 of Nambara abstract), which constitute *R*- ( $\alpha$ ) and *S*- ( $\beta$ ) enantiomers of 2-methoxy-3-hydroxy-16-chloro-estra-1,3,5(10)-trien-17-one. However, Applicants note that the March 13, 2002 Office Action also refers to the reference compound that contains  $R_a = O-R$ , where  $R = aralkyl$  (paragraph 2, line 4), perhaps indicating the Examiner's intention to cite compounds RN 54502-35-1 and 54502-32-8 (shown on page 13 of Nambara abstract) against Claims 1, 2 and 8. In the interest of advancing the prosecution of this application, Applicants distinguish their invention from both sets of compounds.

RN 54502-29-3 and 54502-31-7:  $\alpha$  and  $\beta$  enantiomers of 2-methoxy-3-hydroxy-16-chloro-estra-1,3,5(10)-trien-17-one. By the amendment entered herein, Applicants incorporate the proviso in Claim 1 that if  $R_b$  is H,  $R_o$  is H,  $R_a$  is OMe,  $Z'$  is  $>COH$ ,  $>C-R_g$  is  $>C=O$ , and  $Z''$  is  $>CH_2$ , then  $R_{h1}$  and  $R_{h2}$  are not collectively H and Cl. This amendment clearly removes the subject matter of Nambara's compounds from Claim 1. Accordingly, Applicants respectfully request removal of this rejection and allowance of Claim 1.

Further, Applicants aver that neither Claim 2 nor Claim 8 in their present form are anticipated by the RN 54502-29-3 and 54502-31-7 of Nambara. Claim 2 specifically defines >C-R<sub>g</sub> as >C(H)-β-OH, rather than >C=O, as disclosed in Nambara. Claim 8 defines R<sub>h1</sub> and R<sub>h2</sub> independently as H and Me, rather than H and Cl, as disclosed in Nambara. Thus, neither Claim 2 nor Claim 8 read on the reference species. Accordingly, Applicants respectfully request removal of this rejection and allowance of Claims 2 and 8.

RN 54502-35-1 and 54502-32-8: α and β enantiomers of 2-phenylmethoxy-3-methoxy-16-chloro-estra-1,3,5(10)-trien-17-one. Applicants respectfully maintain that none of Claims 1, 2 or Claim 8 is anticipated by RN 54502-35-1 and 54502-32-8 (page 13) of Nambara. Specifically, none of these claims provides for compounds where Z' is >COMe, as required by the reference compounds. Accordingly, Applicants respectfully request removal of this rejection and allowance of Claims 1, 2 and 8.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments in the Specification:

In accordance with 37 CFR 1.121(b), the following replacement paragraphs show all the changes made by the foregoing amendment relative to the previous version of the paragraphs.

Page 22, First (1<sup>st</sup>) Full Paragraph

b) R<sub>a</sub> is -N<sub>3</sub>, -C≡N, -C≡C-R, -CH=CH-R, -R-CH=CH<sub>2</sub>, -C≡CH, -O-R, -R-R<sub>1</sub>, -OC(O)CH<sub>3</sub>, -C(O)H, -NH<sub>2</sub>, -NMe<sub>2</sub>, -NHMe, or -O-R-R<sub>1</sub> where R is a straight or branched alkyl with up to 10 carbons or aralkyl, and R<sub>1</sub> is -OH, -NH<sub>2</sub>, -Cl, -Br, -I, -F or CF<sub>3</sub>;

Page 22, Fourth (4<sup>th</sup>) Full Paragraph

e) R<sub>h1</sub> and R<sub>h2</sub> are independently H, or a straight or branched chain alkyl, alkenyl or alkynyl with up to 6 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality (O-Y, N-Y<sub>2</sub> or S-Y) where Y is independently selected from H, Me or an alkyl chain up to 6 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with hetero, halo or alkyl; or R<sub>h1</sub> and R<sub>h2</sub> are independently an aromatic group optionally substituted with hetero, halo or alkyl, provided that both R<sub>h1</sub> and R<sub>h2</sub> are not H;

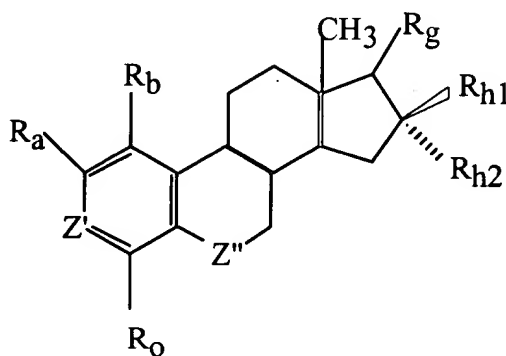
Page 22, Fifth (5<sup>th</sup>) Full Paragraph

f) Z'' is >CH<sub>2</sub>, >C=O, >C(H)-OH, [>C=N-OH,] >C=N-OR<sub>5</sub>, >C(H)-C≡N, or >C(H)-NR<sub>5</sub>R<sub>5</sub>, wherein each R<sub>5</sub> is independently hydrogen, an alkyl or branched alkyl with up to 10 carbons or aralkyl;

Amendments in the Claims

In accordance with 37 C.F.R. § 1.121(c), the following version of the rewritten claims shows all the changes made by the foregoing amendment relative to the previous version of the claims.

1. (Amended) A compound of the general formula:



wherein:

a)  $R_b$  and  $R_0$  are independently -H, -Cl, -Br, -I, -F, -CN, lower alkyl, -OH, -CH<sub>2</sub>-OH, -NH<sub>2</sub>; or N( $R_6$ )( $R_7$ ), wherein  $R_6$  and  $R_7$  are independently hydrogen or an alkyl or branched alkyl with up to 6 carbons;

b)  $R_a$  is -N<sub>3</sub>, -C≡N, -C≡C-R, -CH=CH-R, -R-CH=CH<sub>2</sub>, -C≡CH, -O-R, -R-R<sub>1</sub>, -OC(O)CH<sub>3</sub>, -C(O)H, -NH<sub>2</sub>, -NMe<sub>2</sub>, -NHMe, or -O-R-R<sub>1</sub> where R is a straight or branched alkyl with up to 10 carbons or aralkyl, and  $R_1$  is -OH, -NH<sub>2</sub>, -Cl, -Br, -I, -F or CF<sub>3</sub>;

c) Z' is  $>\text{CH}$ ,  $>\text{COH}$ , or  $>\text{C-R}_2\text{-OH}$ , where  $\text{R}_2$  is an alkyl or branched alkyl with up to 10 carbons or aralkyl;

d)  $>\text{C-R}_g$  is  $>\text{CH}_2$ ,  $>\text{C(H)-OH}$ ,  $>\text{C=O}$ ,  $>\text{C=N-OH}$ ,  $>\text{C(R}_3\text{)OH}$ ,  $>\text{C=N-OR}_3$ ,  $>\text{C(H)-NH}_2$ ,  $>\text{C(H)-NHR}_3$ ,  $>\text{C(H)-NR}_3\text{R}_4$ , or  $>\text{C(H)-C(O)-R}_3$ , where each  $\text{R}_3$  and  $\text{R}_4$  is independently an alkyl or branched alkyl with up to 10 carbons or aralkyl;

e)  $\text{R}_{h1}$  and  $\text{R}_{h2}$  are independently H, or a straight or branched chain alkyl, alkenyl or alkynyl with up to 6 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality ( $\text{O-Y}$ ,  $\text{N-Y}_2$  or  $\text{S-Y}$ ) where Y is independently selected from H, Me or an alkyl chain up to 6 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with hetero, halo or alkyl; or  $\text{R}_{h1}$  and  $\text{R}_{h2}$  are independently an aromatic group optionally substituted with hetero, halo or alkyl, provided that both  $\text{R}_{h1}$  and  $\text{R}_{h2}$  are not H;

f) Z'' is  $>\text{CH}_2$ ,  $>\text{C=O}$ ,  $>\text{C(H)-OH}$ , [ $>\text{C=N-OH}$ ,]  $>\text{C=N-OR}_5$ ,  $>\text{C(H)-C}\equiv\text{N}$ , or  $>\text{C(H)-NR}_5\text{R}_5$ , wherein each  $\text{R}_5$  is independently hydrogen, an alkyl or branched alkyl with up to 10 carbons or aralkyl;

[and] wherein all monosubstituted substituents have either an  $\alpha$  or  $\beta$  configuration, and with the proviso that if  $\text{R}_b$  is H,  $\text{R}_o$  is H,  $\text{R}_a$  is OMe, Z' is  $>\text{COH}$ ,  $>\text{C-R}_g$  is  $>\text{C=O}$ , and Z'' is  $>\text{CH}_2$ , then  $\text{R}_{h1}$  and  $\text{R}_{h2}$  are not collectively H and Cl.



9. (Amended) The compound of Claim 1, wherein:

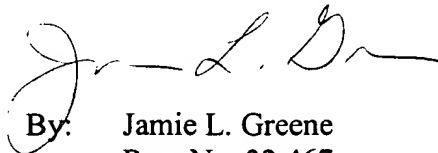
$R_{h1}$  and  $R_{h2}$  are independently H and  $(CH_2)_n[-C]N(Me)_2$ , wherein  
n is from 1 to 6.

New Claims 11-30 have been added.

**Conclusion**

By this Amendment and Response, Applicants have amended Claims 1 and 9, and added new Claims 11-30. Corresponding amendments to the specification are also entered. Applicants believe that the claims now are in condition for allowance. A Notice of Allowance is therefore respectfully solicited. If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 815-6500 is respectfully solicited.

Respectfully submitted,

  
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